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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/746,635	11/13/1996	VADIRAJA MURTHY	96700/341	7843

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 11/24/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	08/746,635	MURTHY ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 November 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 2 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *NONE*.

   Claim(s) objected to: *NONE*.

   Claim(s) rejected: *20 and 24-46*.

   Claim(s) withdrawn from consideration: *NONE*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 11/4/03 in Paper No. 44 is acknowledged and has been entered. Claims 20 and 24 have been amended. Currently, claims 20 and 24-26 are pending and are under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

2. Claim 20 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Olsson et al. (Journal of Applied Biochemistry, 5:437-445 (1983)) for reasons of record in Paper No. 36 and 43.

3. Claims 24-26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Olsson et al. (Journal of Applied Biochemistry, 5:437-445 (1983)) as applied to claim 20 above, and further in view of Matsura et al. (Journal of Biological Chemistry, 264 (17): 10148-10155 (1989)) for reason of record in Paper No. 43.

Response to Arguments

4. Applicant's arguments filed 11/4/03 have been fully considered but they are not persuasive.

A) Applicant argues that Olsson does not suggest the claimed method for diagnosing erythrocyte hemolysis in a subject wherein "the presence of *at least about 20 U/L erythrocyte adenylate kinase activity* in a serum sample obtained from the subject is indicative of erythrocyte hemolysis in a subject". Applicant specifically contends that in Table 1 of Applicant disclosure, it is clearly indicated that low levels of adenylate kinase activity can be present in the absence of hemoglobin; thus there is a threshold for erythrocyte adenylate kinase activity, above which erythrocyte kinase activity is indicative of erythrocyte hemolysis. Applicant thus maintains that Olsson does not suggest the need to determine the threshold level of erythrocyte kinase activity because Figure 6 in Olsson indicates that there is no threshold; thus it teaches away

from the claimed invention. Applicant contends that the claimed invention achieved an unexpected result relative to the teachings of Olsson.

In response, Olsson et al. found that that there was a high degree of correlation between the amount of accumulated hemoglobin and adenylate kinase. Olsson et al. provided the relationship of adenylate kinase in Figures 6A, 6B, and 6C: 1) with packed red cell levels having *increased hematocrit* in Figure 6A and 6B showing *increased level of adenylate kinase activity from elevated amounts of hemoglobin (a known indicator of hemolysis)*; in comparison to 2) whole blood having *decreased hematocrit* in Figure 6C showing *reduced adenylate kinase activity from decreased amount of hemoglobin*. Olsson et al. showed the parallel correlation in ratio between (decreasing) adenylate kinase and (decreasing) hemoglobin that has remained relatively constant. Accordingly, to obtain the minimal relational parameters between hemoglobin, i.e. 1 g/L, and its corresponding level of adenylate kinase activity, i.e. 21 U/L or 22 U/L to thus, define a minimum threshold value in the correlative relationship between hemoglobin, i.e. hemolysis, and adenylate kinase, only requires optimization procedures and within conventional practice. Additionally, it is further known that adenylate kinase is also present in platelets, skeletal muscle, etc. (as per Olsson and Matsura) which accounts for some degree of adenylate kinase activity not resulting from hemolysis or hemoglobin. Therefore, Applicant's argument that the value obtained and recited in the claimed invention is an "unexpected result", is not persuasive.

5. Applicant's arguments have been considered but are not deemed persuasive.

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641

Gailene R. Gabel
Art 1641
November 20, 2003